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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/627,775	07/28/2000	Mark I. Greene	UPN-3832	3099

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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/27/2002 22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/627,775	Greene
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 15, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *2, 3, 5-16, 18-30, 34, 35, and 37-48* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *2, 3, 5-16, 18-30, 34, 35, and 37-48* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Continued Examination Under 37 CAR 1.114

1. A request for continued examination under 37 CAR 1.114, including the fee set forth in 37 CAR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CAR 1.114, and the fee set forth in 37 CAR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CAR 1.114. Applicant's submission filed on has been entered.

Specification

2. Claims 4 and 36 have been canceled without prejudice towards further prosecution. Claims 2, 5, 9, 13, 15, 18-19, 23, 27, 34, 37, 41, and 45 have been amended.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 2, 3, 5-16, 18-30, 34, 35, and 37-48 are rejected under 35 U.S.C. 103 (a) over Yamaguchi et al. (Journal of Biological Chemistry, (1998), Vol. 273 (No: 9), pages 5117-5123) in view of Green et al. (PCT International Publication NO: WO 98/53842) (December 3, 1998) further in view of Kwon et al. (The FASEB Journal, (1998), Vol. 12, pages 845-854).

Yamaguchi et al teach a method for inhibiting osteoclastogenesis, and bone loss by reciting that osteoclastogenesis inhibitory factor (OCIF) is a heparin-binding secretory glycoprotein that belongs to the tumor necrosis factor (TNF) family. OCIF is present both as a ~ 60 kDa monomer and a disulfide-linked homodimer. Their result show that the N-terminal portion of OCIF containing domains 1-4, which have structural similarity to the extracellular domains of the TNFR family proteins, is sufficient to inhibit osteoclastogenesis (Abstract, Figures 1-2, page 5119).

Yamaguchi et al do not teach the peptide inhibitors with 3-18, 1-6, 1-3, and 1-2 amino acids.

Green et al teach the peptide inhibitors with 3-18, 1-6, 1-3, and 1-2 amino acids (Page 4, lines 21-36, and page 5, lines 1-19). Green et al also teach the composition of an inhibitor which

has a peptide of 3-18 amino acid residues corresponding in primary sequence to a binding loop of a TNF-R superfamily member with all the limitation of the claimed invention. Moreover, Green et al teach an inhibitor which has the identical skeletal structure with a peptide of 1-6 amino acids, at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroatomic moiety which has all the limitations of the claimed invention (Page 23, lines 25-36, and page 25, lines 1-14, and page 27).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the composition of an inhibitor which has a peptide of 3-18 amino acid residues corresponding in primary sequence to a binding loop of a TNF-R superfamily member of Green et al. in the method of osteoclastogenesis inhibition of Yamaguchi et al., since Green et al. state, "The present invention relates to peptides and peptide analogues designed from a binding loop of a member of the tumor necrosis factor receptor (TNF-R) superfamily, which is involved in binding interactions with its ligand. In particular, it relates to cyclic peptides and peptide analogues designed from three specific binding loops in domains 2 and 3 of TNF-R which inhibit tumor necrosis factor (TNF) binding to its cellular receptors, methods of designing similar peptides and peptide analogues, and methods of using such compounds to inhibit the biological activities of TNF, thereby antagonizing its undesirable clinical effects" (Introduction, lines 5-15). Moreover, Yamaguchi et al provides motivation as Yamaguchi et al state, "The N-terminal portion of OCIF containing domains 1-4, which have structural similarity to the extracellular domains of the TNFR family proteins, is sufficient to

inhibit osteoclastogenesis (Abstract, lines 12-15)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the composition of an inhibitor which has a peptide of 3-18 amino acid residues corresponding in primary sequence to a binding loop of a TNF-R superfamily member of Green et al. in the method of osteoclastogenesis inhibition of Yamaguchi et al. in order to achieve the express advantages, as noted by Yamaguchi et al., of an invention that reveals the effectiveness of the N-terminal portion of OCIF containing domains 1-4, which have structural similarity to the extracellular domains of the TNFR family proteins, to inhibit osteoclastogenesis.

Yamaguchi et al. in view of Green et al do not teach the receptor TNF-R(I).

Kwon et al teach the receptor TNF-R(I) and a TR1 receptor similar to TNF-R(I) having inhibitory activity of osteoclastogenesis (Introduction Section, first paragraph, Figure 1C).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the receptor TNF-R(I) and a TR1 receptor similar to TNF-R(I) having inhibitory activity of osteoclastogenesis of Kwon et al. in the method of osteoclastogenesis inhibition of Yamaguchi et al in view of Green et al since Kwon et al. state, "Examples include CD40, 4-1BB, TNFR-I, TNFR-II, Fas, as well as other recently described members, and several viral open reading frames. Recent studies have shown that these molecules are involved in diverse biological activities such as immunoregulation, cell proliferation, cell survival, and death (Introduction Section, first paragraph)". Moreover, Kwon et al further state, "We found that the molecule exhibited broad biological activities, including

fibroblast proliferation, inhibition of osteoclastogenesis, and inhibition of bone resorption (Introduction, last sentence)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the receptor TNF-R(I) and a TR1 receptor similar to TNF-R(I) having inhibitory activity of osteoclastogenesis of Kwon et al. in the method of osteoclastogenesis inhibition of Yamaguchi et al in view of Green et al. in order to achieve the express advantages, as noted by Kwon et al., of an invention which provides TNFR-I, TNFR-II, Fas, as well as other recently described members, and several viral open reading frames which are involved in diverse biological activities such as immunoregulation, cell proliferation, cell survival, and death as well as broad biological activities, including fibroblast proliferation, inhibition of osteoclastogenesis, and inhibition of bone resorption.

Response to Amendment

5. In response to amendment, all previous 112 (second paragraph) and 103 (a) rejection have been withdrawn. However, a new 103 (a) rejection has been included.

Response to Arguments

6. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti
Patent Examiner
Art Unit 1634

December 6, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600